Ph.D. Dissertation Defense

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Room 1345, Health Sciences Learning Center

"Advancing Intact Protein Analysis by Top-down Mass Spectrometry"

The study of proteins is critical for understanding cellular functions at the molecular level. Top-down mass spectrometry (MS), which analyzes intact proteins without digestion, has emerged as a premier tool for global and comprehensive study of proteoforms (all protein forms arise due to genetic variants, alternative splicing, and post translational modifications (PTMs) from a given gene). The top-down approach not only retains intact mass information, providing a "bird's-eye" view, but also allows for identification of novel proteoforms, in-depth sequence characterization, and quantification of disease associated PTMs. However, many technical challenges still exist for the top-down approach. In this presentation, I will discuss my efforts in advancing intact protein analysis by top-down MS in the areas of enrichment, separation, and characterization. Specifically, I will present functionalized nanoparticle aided phosphoprotein enrichment, online hydrophobic interaction chromatography-MS, and how these techniques can be applied to characterize samples ranging from complex lysates to large therapeutic biomolecules. Overall, these analytical developments expand the toolbox of the top-down approach and facilitate the analysis of intact proteins in general.